Epidemiol. Infect. (1998). **121**, 609–614. Printed in the United Kingdom © 1998 Cambridge University Press

Low rates of ehrlichiosis and Lyme borreliosis in English farmworkers

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(*Accepted 15 July 1998*)

SUMMARY

To determine the occupational significance of tick-borne zoonoses we sought serological evidence of Lyme borreliosis, human monocytic ehrlichiosis (HME) and human granulocytic ehrlichiosis (HGE) in a representative sample of farmworkers. Although around 20% reported ticks on their domestic and companion animals, few (< 2% per year) reported being bitten by ticks. Seroprevalence of Lyme borreliosis (0·2%), HME (0·2%) and HGE (1·5%) was low. Those seropositive for HGE were no more likely to report tick bites nor more likely to report ticks on their animals. This study provides evidence that farmworkers in England are exposed to tick-borne zoonoses but that they are uncommon. Since the severity of these diseases is linked to delays in diagnosis and treatment, clinicians should be aware of these diagnoses in patients from rural communities, with or without a self-reported history of tick bite.

INTRODUCTION

Human monocytic ehrlichiosis, human granulocytic ehrlichiosis (HGE) and Lyme borreliosis are emerging tick-borne zoonoses [1–3]. Whereas ixodid ticks are common in the United Kingdom [4] indigenous cases of Lyme borreliosis are uncommon; 51 clinical cases were reported to the Public Health Laboratory Service Communicable Disease Surveillance Centre by laboratories in England and Wales in 1996, of which at least five were probably acquired overseas (R. M. M. Smith, personal communication), and there are no known clinical reports of human ehrlichiosis in the UK. We sought serological evidence of infection in a representative population of farmworkers from three areas of England, a sentinel group exposed to wildlife, domestic animals and ticks through their occupation.

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METHODS

Subjects

In an ongoing cohort study of zoonotic illness in farmworkers and their families, a sample of 404 people was recruited in 1991 from 255 farms randomly selected from Ministry of Agriculture Fisheries and

Food (MAFF) lists of agricultural holdings for the English local government districts of Hereford City, South Hereford, Leominster, Preston and Lancaster (group 1) [5, 6]. Since 1991 participants have provided a 10 ml venous blood sample each year and have completed administered questionnaires. In 1995, in an extension to this study, a group of farmworkers and their families in a third region of the UK (202 participants from 137 holdings in the local government districts of Broadland, Breckland and South Norfolk) were recruited by the same method (group 2) [7]. Both groups were characterized in terms of medical and veterinary history, and animal and other occupational exposures. Self reported exposure to ticks was recorded for groups 1 and 2 and exposure to deer was recorded for group 1. Occupation and farm-type of participants were coded as in the June Census. Sampling, recruitment, and measurement of exposure are described elsewhere [5].

Lyme borreliosis serology

Group 1 samples taken at enrolment ($n = 404$) and at 1 ($n = 387$), 2 ($n = 345$), and 3 years ($n = 336$) post enrolment and group 2 samples taken at enrolment ($n = 137$) were screened for IgG antibodies to *Borrelia burgdorferi* at Hereford Public Health Laboratory (PHL) by a commercial enzyme-linked immunosorbent assay (ELISA) test kit (Dako) using native *B. burgdorferi* flagellum as antigen. Provisional positives were confirmed using a second commercial IgG ELISA (Sigma) at Hereford PHL and by Western blot at the Lyme Disease Reference Laboratory, Southampton PHL.

Ehrlichiosis serology

Sera from 518 subjects in group 1 at 2 years post enrolment ($n = 345$) and group 2 at enrolment ($n = 173$) were examined for IgG antibody to *E. chaffeensis*, the cause of human ehrlichiosis, by immunofluorescence assay (IFA) using *E. chaffeensis*-infected canine mononuclear cells as antigen. Titres of 64 or higher were considered indicative of *E. chaffeensis* infection [8]. Sera from group 1 and group 2 were also examined at MRL Reference Laboratory, California (licensed reference laboratory for diagnostic laboratories in the USA), for IgG antibody to human granulocytic ehrlichiosis by indirect immunofluorescence assay (IFA) using HL 60 cells infected with a human strain of granulocytic ehrlichiosis. Titres of 64 or higher were considered positive.

Analysis

Prevalence rates were expressed as the number of seropositives and incidence as the number of new seropositives per year per 100000 population employed in agriculture in England. Ninety-five per cent confidence intervals (CI) were calculated for rates assuming a Poisson distribution using STATA 5 [9]. Those seropositive were described in terms of age, gender, occupation, farm-type, animal exposures and other occupational exposures, including tick bites. Odds ratios and 95% CIs were calculated by logistic regression using STATA 5. Prevalence of HGE in groups 1 and 2 was compared using the Fisher exact method for the χ^2 test and the distribution of *E. chaffeensis* antibody titres in HGE positives and negatives were compared using the Mann–Whitney *U* test in Epi Info 6 [10].

RESULTS

Five of the 393 subjects in group 1 (1·3%) reported a history of tick bites in the year following enrolment (3 male, 2 female), 1/347 (0·3%) in the second year following enrolment (male) and 1/337 (0·3%) in the third year following enrolment (male). Four of the 202 subjects in group 2 (2·0%) reported a history of tick bites in the first year following their enrolment (3 male, 1 female). Seventy-five subjects in group 1 (19·1%) reported tick bites on their domestic and/or companion animals in the year following enrolment, 77 (22·2%) in the second year following enrolment and 64 (19·0%) in the third year following enrolment. Thirty-three of 129 subjects in group 2 (25·6%) reported tick bites on their animals in the first year following their enrolment. Dogs were the animal species on which ticks were most frequently observed. Other species reported as having ticks were cats, sheep, cattle and pigs.

At enrolment 31 subjects in group 1 were positive for antibodies to *B. burgdorferi* by ELISA. However seropositivity of only one of these participants was confirmed by Western blot, equivalent to a seroprevalence rate of 247·5 (95% CIs 6·3–1379·1). This antibody-positive participant was male, aged between

Table 1. *Person details and prevalence of IgG antibodies to human granulocytic ehrlichiosis (HGE) (cut-off: titre 64 or over) in farmworkers and their families*

	Unadjusted		
Exposure	Prevalence	OR	95% CI
Sex			
Male	8/384	1.00	—
Female	0/134	—	
Age group			
< 30	1/64	1·00	—
30–39	0/108	—	
40–49	3/150	1.29	0·13–12·60
50–59	2/137	0·93	0·08–10·49
60+	2/59	2·21	0·20–25·04
Study site			
Hereford	3/171	1.00	—
Preston	4/174	1·32	0·29–5·98
Norwich	1/173	0·33	0·03–3·16
Occupation			
Principal farmer	7/368	1·00	—
Spouse	1/77	0·68	0·08–5·60
Manager	0/4	—	
Other family workers	0/28	—	
Regular hired workers	0/23	—	
Other	0/18	—	
Full-time employed			
Part-time	1/56	1·00	—
Full-time	7/461	0·87	0·10–7·15
Farm type			
Cereals/horticulture	1/61	1·00	—
Specialist dairy	1/27	2·31	0·14–38·32
Mainly dairy	2/138	0·88	0·08–9·92
Livestock mainly cattle	0/26	—	
Livestock mainly sheep	0/37	—	
Livestock sheep and cattle	2/82	1·50	0·13–16·93
Poultry/pigs	0/52	—	
Mixed	2/89	1·38	0·12–15·56
Other	0/5	—	

40 and 50 years and reported exposure to sheep (155 in flock), cattle (34), chickens (3), dogs (2) and rats. The participant did not report a history of tick bits in the 3 years following enrolment (no data available on tick bits prior to enrolment), nor ticks on his domestic animal contacts.

Slightly less than half (48·9%) of group 1 reported deer on their land. However the one seropositive participant reported no deer on the farmland. No clinical history of Lyme disease was reported by any subject. The seropositive participant reverted to seronegative when tested 12 months later and remained negative in subsequent samples. No seroconversions were observed during the study period, giving an incidence rate of 0/100, 000 per year (95% CIs 0–955·3 in the first year, 0–1072·0 in the second year and 0–1100·8 in the third year. One of the 137 participants in group 2 tested antibody positive by ELISA but seropositivity was not confirmed positive by Western blot.

Of 518 participants tested in groups 1 and 2, one was positive for *E. chaffeensis* IgG antibody (titre: 64) equivalent to a seroprevalence of 193·1 (95% CIs 4·9–1075·6). Ten other participants had equivocal results (eight were at titre 16, two at titre 32).

The one antibody-positive subject was a male full-time principal farmer aged between 40 and 50 years who reported exposure to sheep (20), goats (2), cattle (3), chickens (12), pigs (2), cats (2), dogs (3) and rats. Other occupational exposures reported were: milking cows by hand, nursing lambs in the home, attending the birth of animals, drinking unpasteurized cows' milk and, until recently, drinking unpasteurized goats' milk. When asked, the participant reported not having been bitten by a tick in the preceding 12 months, had not noticed ticks on any of his animals, and had no history of overseas travel (defined as spending a period longer than 6 weeks overseas).

Eight subjects tested positive (six at titre 64, two at titre 128) for antibody to human granulocytic ehrlichiosis (equivalent to a seroprevalence of 1544·4, 95% CIs 666·8–3042·9), 7/345 from group 1 and 1/173 from group 2 ($P > 0·05$). All eight subjects were male with ages ranging from 30–68 years. Prevalence did not increase with age and though prevalence was highest in those who worked or lived on a specialist dairy farm (3·7%) this was not significant (OR 2·38, 95% CI 0·14–39·58) (Table 1). Positives were less likely to report contact with sheep (OR 0·01, 95% 0·00–0·51, adjusted for other animal exposures and person details) (Table 2). Four people who reported a tick bite in the previous 12 months were seronegative, and only 1 of the 107 who reported observing ticks on their animals in the previous 12 months was positive compared with 7/363 not reporting a sighting (OR 0·48, 95% CI 0·06–3·91). Seropositives were more likely to drink unpasteurized cows' milk, although this finding was not significant (OR 2·12, 95% 0·50–8·96), but were no more likely to be exposed to rats, or drink unpasteurized goats' milk (Table 3).

The subject who tested positive for *B. burgdorferi* was negative for HGE and *E. chaffeensis*. The person who tested positive for *E. chaffeensis* tested negative for HGE, but a trend was observed in which those

Table 2. *Exposure to domestic animals and prevalence of HGE antibodies (cut-off: titre 64 or over) in farmworkers and their families*

Exposure (Yes/no)	Prevalence		Unadjusted		Adjusted for other animal exposures in table and person details*	
	Not exposed	Exposed	OR	95% CI	OR	95% CI
Cattle	1/130	7/388	2·37	0·29–19·45	2·45	0·04–152·9
Sheep	4/194	4/324	0·56	0·12–2·60	0·00	0·00–0·60
Goats	8/497	0/21	—	—	—	—
Pigs	8/434	0/84	—	—	—	—
Dogs	2/77	6/439	0·54	0·09–3·30	0·23	0·02–2·37
Cats	3/211	5/305	1·14	0·31–5·96	1·33	0·19–9·49
Horses	8/403	0/115	—	—	—	—
Chickens	7/375	1/143	0·56	0·07–4·79	—	—
Turkeys	8/504	0/14	—	—	—	—
Ducks	8/584	0/34	—	—	—	—
Geese	8/491	0/27	—	—	—	—

* Sex, age group, study site, occupation, full-time employed and farm type.

Table 3. *Effects of other occupational exposures on prevalence of HGE antibodies in farmworkers and their families*

Exposure (Yes/no)	Prevalence		Unadjusted	
	Not exposed	Exposed	OR	95% CI
Tick bite	8/513	0/4	—	
Animals bitten by ticks	7/363	1/107	0·48	0·06–3·91
Handling rats	7/414	1/104	0·59	0·07–4·82
Rat problem on the farm	8/452	0/66	—	
Deer on land	3/175	4/169	1·39	0·31–6·30
Drinking raw cows' milk	3/279	5/239	2·12	0·50–8·96
Drinking raw goats' milk	8/506	0/12	—	

positive for HGE had higher antibody titres to *E. chaffeensis* (mode 16, median 16, range 0–32 *vs.* mode 0, median 0, range 0–64; $P < 0{\cdot}01$).

DISCUSSION

Human monocytic ehrlichiosis (HME), human granulocytic ehrlichiosis (HGE) and Lyme borreliosis are established as tick-borne zoonoses in Europe. Cases of HME, the clinical syndrome associated with *E. chaffeensis* infection, have been reported from Portugal [11], Spain and Belgium [12]. Serological evidence of infection by the HGE-agent, an *E. phagocytophila*-like ehrlichia, has been demonstrated in Switzerland [13], United Kingdom [14], Norway [15], Sweden [16], Italy [17] and Slovenia [18] and *B. burgdorferi s.l.*, the agent of Lyme disease, is widely distributed in ticks and wild animal reservoirs across Europe [19]. However the importance of these diseases is still unclear [20].

This study provides evidence that farmworkers in England are indeed exposed to the agents of human monocytic ehrlichiosis, human granulocytic ehrlichiosis and Lyme borreliosis. Clinicians should be aware of this as the diseases are treatable. They are however rare.

Lyme disease serology is generally used to support a clinical diagnosis. In the absence of clinical illness these serology data must therefore be interpreted with caution. We found low rates of exposure. Though *B. burgdorferi* s.l. is found in areas throughout the UK, rates of reported human disease are low outside a

small number of foci of infection, for example the New Forest and Thetford Forest [3]. Although Breckland local authority area, included in our sampling frame, encompasses part of Thetford Forest, only one farm enrolled in this study was located in Thetford Forest. Subjects from this farm were seronegative to HME, HGE and Lyme borreliosis.

The low incidence of Lyme borreliosis in the UK is thought to be related to the low intensity of *B. burgdorferi* s.l. infection observed in UK *I. ricinus* ticks [21] and the relatively low prevalence of infection in the nymphal stage of the ticks compared to that observed in the USA [22–24]. As adult ticks are considerably less numerous than nymphs and more easily detected before they transmit infection, the probability of humans acquiring infection in the UK is therefore thought to be relatively low, compared with the USA and mainland Europe.

Prevalence of granulocytic ehrlichia infection in *I. ricinus* ticks in UK woodlands also seems to be lower than in woodlands in the USA, most likely associated with different dynamics of ticks and reservoir host species [25]. In many UK uplands, however, the main host species for adult and immature *I. ricinus* are sheep and cattle, both known to be competent reservoirs of granulocytic ehrlichiae. Consequently in the uplands prevalence of infection in ticks may be higher than in woodlands and risk of human infection following a tick bite may be greater.

Twenty percent of the cohort reported observing ticks on their animals but the incidence of reported human tick-bite was low (0·8% per year). This low incidence of human tick-bites could be due to an increased awareness of ticks in this cohort and the wearing of protective outdoor clothing. Conversely, feeding nymph and larval ticks may not be detected and therefore not reported. Evidence would suggest that the ticks' ability to modulate host immune and inflammatory responses may decrease its chance of detection [26]. Those seropositive for any tick-borne zoonosis were male; this is not explained by the distribution of tick bites. Indeed, in this study there appeared to be no relationship between self-reported tick bite and being positive for HGE, HME or Lyme borreliosis, raising the question as to the usefulness of a history of tick bite in the differential diagnosis of these zoonoses by clinicians.

In this study subjects who reported ticks on their domestic animals were no more likely to have deer on their land (OR 0·96, 95% CI 0·56–1·64). The presence of deer, reported by half of the cohort, did not appear to increase the burden of ticks on farmed land. Although the rate of tick bites was higher in those farmworkers exposed to sheep, rates of HGE were significantly lower in those reporting contact with sheep. Contact with sheep *per se* may not be a risk factor for acquiring HGE, particularly in lowland areas where sheep are exposed to fewer ticks and less agent. Unfortunately data were not available on sheep husbandry practices on farms included in the study. Previous UK studies have found high rates of *B. burgdorferi* exposure in cattle farmers [27, 28]. Though odds of being HGE antibody positive were higher in those exposed to cattle, this finding was not statistically significant. The role of domestic animals in the epidemiology of tick-borne zoonoses, and in particular HGE, warrants further investigation as does the risk of infection in other population groups exposed to ticks.

ACKNOWLEDGEMENTS

We thank Sue O'Connell, Southampton Public Health Laboratory, UK, The Binding Site, Birmingham, UK, The Microbiology Reference Laboratory (MRL), Cypress, California, United States. This work was funded by the UK Health and Safety Executive and by the Public Health Laboratory Service.

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